DEPARTMENT OF THE ARMY

CHEMICAL BIOLOGICAL MEDICAL SYSTEMS JOINT PROJECT MANAGEMENT OFFICE

BROAD AGENCY ANNOUNCEMENT

MEDICAL CHEMICAL BIOLOGICAL RADIOLOGICAL AND NUCLEAR COUNTERMEASURE RESEARCH AND DEVELOPMENT

AREAS OF INTEREST

BAA 07-01

AUGUST 2007

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FREDERICK, MARYLAND

CHEMICAL BIOLOGICAL MEDICAL SYSTEMS JOINT PROJECT MANAGEMENT OFFICE

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PREFACE

Medical Chemical, Biological, Radiological and Nuclear (CBRN) countermeasures are an integral part of the U.S. Department of Defense (DoD) Chemical Biological Defense Program (CBDP) System of Systems approach that serves as the foundation and strength of the CBDP. The Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) is organized into eight Joint Project Management Offices, each responsible for specific commodity areas. The Chemical Biological Medical Systems Joint Project Management Office (CBMS JPMO) consists of the Joint Vaccine Acquisition Program (JVAP), Medical Identification and Treatment Systems (MITS), and Transformational Medical Technologies Initiative (TMTI) Joint Product Management Offices (JPMOs). The medical CBRN countermeasures developed by the CBMS JPMO directly support the current, near-term, and far-term challenges by providing the capability to prevent, diagnose and treat the effects of chemical, radiological and biological warfare agents. The JVAP JPMO provides biological protection by ensuring Warfighters' immune systems are primed to protect them from selected threats. The MITS JPMO is responsible for the advanced development of U.S. Food and Drug Administration (FDA)-approved/licensed/cleared products for prophylaxis, treatment and diagnosis of CBRN agent exposure. The TMTI JPMO is developing and evaluating novel processes to accelerate the development and approval of medical CBRN countermeasures by leveraging lifecycle bioinformatics, enabling technologies, and other emerging technologies. General information on JPEO-CBD and subordinate JPMOs can be obtained from the JPEO-CBD website at http://www.jpeocbd.osd.mil/.

This Broad Agency Announcement (BAA) is intended to solicit pre-proposals for: 1) those parts of development not related to the development of a specific system or hardware procurement in accordance with (i) the Federal Acquisition Regulation (FAR) 35.016(a) and (ii) DoD Grant Regulations (DoDGARs) subject to section 2374 of Title 10 United State Code and 2) the development of prototypes in accordance with Section 845 of Public Law (P.L.) 103-160. The purpose of this BAA is to identify the best available science, and as such, there are no set-asides associated with any awards resulting from this BAA. Specific areas of interest are described in the "Areas of Interest" attachment. As to any resultant procurement contracts, this BAA is issued under the provisions of the Competition in Contracting Act of 1984 (P.L. 98-369), as implemented in the FAR at accordance. This Announcement provides a general description of the JPEO-CBD and CBMS JPMO's project areas, including specific areas of interest, general information, evaluation and selection criteria, and proposal preparation instructions. All Attachments that are required with the submission of a full proposal are described in the Mandatory Proposal Forms section of this announcement. **Proposals are sought from all eligible sources, including educational institutions, nonprofit organizations, and private industry. Generally, this announcement is continuously open; preliminary proposals**

(preproposals) may be submitted and will be evaluated at any time throughout the year. The availability of funds may limit the ability of the U.S. Government to make awards in specific areas, nevertheless preproposals are sought under this BAA announcement for all areas of interest described in the "Areas of Interest".

This announcement of the U.S. Government's current interests will be posted on the Grants.gov web portal (http://www.grants.gov/), the Federal Business Opportunity website (http://www.fedbizopps.gov), and the JPEO-CBD website. From time to time, this BAA may be amended with announcements or calls for proposals. Additionally, the application process may be amended as other electronic application processes are implemented. All amendments to this BAA will be announced on the JPEO-CBD website, the Grants.gov web portal, and the Federal Business Opportunity website.

White papers pertaining to grant proposals should not be submitted prior to August 15, 2007.

To facilitate communication on both scientific and administrative matters relating to this BAA, a single email address may be used for all communication with the JPEO-CBD and CBMS JPMO. Please send all technical and administrative questions and inquiries to cbmsbaa@amedd.army.mil.

Potential applicants are encouraged to discuss their proposal ideas with the CBMS technical staff. In addition to the address above, potential applicants may discuss their ideas with the Technical Contacts listed at the end of each area of interest.

Administrative questions concerning the preparation of preproposals or proposals should be addressed to U.S. Army Space and Missile Defense Command (USASMDC)/CBMS JPMO Grants Officer. They should be emailed to cbmsbaa@amedd.army.mil, faxed to 301-619-5069, ATTN: BAA 07-01, or mailed to the following address:

Chemical Biological Medical Systems
ATTN: BAA 07-01
64 Thomas Johnson Dr.
Frederick, MD 21702

Issues with submitting applications through the Grants.gov web portal should be directed to the Grants.gov help desk at 1-800-518-4726 or email support@grants.gov. The Contact Center hours of operation are Monday-Friday, 7 AM to 9 PM Eastern Standard Time.

The Catalog of Federal Domestic Assistance (CFDA) can be accessed online at http://www.cfda.gov. The online CFDA provides access to a database of all Federal programs available to the grant community, including state, local and tribal Governments, academia and research institutions, commercial firms and not-for-profits. Included on the web site are contact information for the office that administers each program, instructions on how to apply for assistance, and several proposal writing guides. The CFDA number for this announcement is 12.360.

CHEMICAL BIOLOGICAL MEDICAL SYSTEMS JOINT PROJECT MANAGEMENT OFFICE

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ACRONYMS

BAA	Broad Agency Announcement
BLA	Biologics License Application
BWA	Biological Warfare Agents
CBDP	Chemical Biological Defense Program
CBMS JPMO	Chemical Biological Medical Systems Joint Project Management Office
CBRN	Chemical, Biological, Radiological, and Nuclear
CFDA	Catalog of Federal Domestic Assistance
CFR	Code of Federal Regulations
cGMP	current Good Manufacturing Processes
CWA	Chemical Warfare Agents
CWVD	Chemical Warfare Vapor Detectors
DoD	Department of Defense
FAR	Federal Acquisition Regulation
FDA	U.S. Food and Drug Administration
GLP	Good Laboratory Practices
IND	Investigational New Drug
JPEO-CBD	Joint Program Executive Office for Chemical and Biological Defense
JVAP JPMO	Joint Vaccine Acquisition Program Joint Product Management Office
MITS JPMO	Medical Identification and Treatment Systems Joint Product Management Office
MRC	Medical Radiation Countermeasure

NDA	New Drug Application
NIOSH	National Institute of Occupational Safety and Health
NTA	Non-Traditional Agents
OT	Other Transaction
OTA	Other Transaction Authority
P.L.	Public Law
RDT&E	Research, Development, Test, and Evaluation
TIC	Toxic Industrial Chemical
TMTI JPMO	Transformational Medical Technologies Initiative Joint Product Management Office
TRL	Technology Readiness Level
USASMDC	U.S. Army Space and Missile Defense Command
USC	U.S. Code

BACKGROUND

GENERAL COMMENTS

The Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) is the Joint Services principal advocate and single focal point for research, development, acquisition, fielding and life-cycle support of chemical and biological defense equipment, systems, and medical countermeasures.

Within the Joint Program Executive Office, eight Joint Project Managers (JPMs) lead, manage, and direct the acquisition and fielding of chemical, biological, radiological and nuclear (CBRN) detection and reconnaissance systems, individual and collective protection systems, decontamination systems, information management systems, medical devices, drugs, and vaccines, and installation and force protection systems.

Located throughout the United States, each JPM office leverages the talents and expertise from across the services under a single chain of command, providing the best chemical and biological defense program (CBDP) technology, equipment and medicine at the right cost, at the right place and at the right time.

The Joint Program Executive Officer (JPEO) provides intensive centralized management of assigned medical and non-medical programs to expedite material solutions for validated CBDP deficiencies. The JPEO monitors technology based activities to promote and facilitate transfer, acceleration, and insertion of emerging technologies to user applications across the military services.

The JPEO supports all military services to include homeland defense, allies, and U.S. citizens and troops abroad. The JPEO establishes and sustains responsive CBDP life cycle management; implements acquisition reform, focused on the use of best practices; maximizes knowledge, technology, and industrial base viability by partnering with government, academic, and commercial organizations to achieve optimal capabilities; enhances user satisfaction to retain and expand its user base; and maximizes employee potential.

This BAA sets forth areas of interest of the JPEO and JPMS

DEFINITIONS

Advanced research. Advanced technology development that creates new technology or demonstrates the viability of applying existing technology to new products and processes in a general way. Advanced research is most closely analogous to precompetitive technology development in the commercial sector (i.e., early phases of research and development on which commercial competitors are willing to collaborate, because the work is not so coupled to specific products and processes that the results of the work must be proprietary). It is typically funded in

Advanced Technology Development (Budget Activity 3 and Research Category 6.3A) programs within Research, Development, Test and Evaluation (RDT&E).

Applied research. Efforts that attempt to determine and exploit the potential of scientific discoveries or improvements in technology such as new materials, devices, methods and processes. It typically is funded in Applied Research (Budget Activity 2 and Research Category 6.2) programs within RDT&E. Applied research normally follows basic research but may not be fully distinguishable from the related basic research. The term does not include efforts whose principal aim is the design, development, or testing of specific products, systems or processes to be considered for sale or acquisition; these efforts are within the definition of "development."

Basic research. Efforts directed toward increasing knowledge and understanding in science and engineering, rather than the practical application of that knowledge and understanding. Basic research is typically funded within Basic Research (Budget Activity 1 and Research Category 6.1) programs within RDT&E.

Development. The systematic use of scientific and technical knowledge in the design, development, testing, or evaluation of potential new products, processes, or services to meet specific performance requirements or objectives. It includes the functions of design engineering, prototyping, and engineering testing. Advanced development consists of activities that plan, produce and deliver information outputs (documents, data, and records) from discovery all the way through Phase 4 post-marketing studies and surveillance. The general phases of the lifecycle are discovery, preclinical and clinical phases

Enabling Technologies. Technologies that are not countermeasure products or systems themselves but facilitate or accelerate the development of countermeasure products or systems. Examples of enabling technologies include combinatorial chemistry, high-throughput screening, microarrays, bioinformatics and computational biology, nanotechnologies, and imaging (including biosensors and biomarkers).

Health Surveillance. The ongoing, systematic collection, analysis, and interpretation of health-related data to detect and assess health risks in order to plan, implement, and evaluate prevention and intervention/response programs. Included are computational models, such as expert systems and predictive models.

Improved Logistics Tracking. Technologies which facilitate tracking and monitoring individual product items throughout shipping, storage, delivery to, and use by the end user (factory to foxhole). For example, technologies which facilitate or simplify cold chain management and/or shelf life extension.

Joint Project Manager (JPM). The designated individual with responsibility for and authority to accomplish program objectives for development, production, and sustainment to meet the user's operational needs. The JPM is accountable for credible cost, schedule, and performance reporting to the MDA.

Life Cycle Bioinformatics. The systematic collection and analysis of data from all phases of research, development, manufacturing, and test and evaluation to enable informed decision making. Included are data obtained from preclinical studies, ensuring compliance with 21 Code of Federal Regulations (CFR) part 11, phase 4/post-marketing studies and product surveillance.

Milestone Decision Authority (MDA) (JPEO-CBD). The designated individual with overall responsibility for the Chemical and Biological Defense Program. The MDA has the authority to approve entry of an acquisition program into the next phase of the acquisition process and shall be accountable for cost, schedule, and performance reporting to higher authority, including Congressional reporting.

THE JOINT PROGRAM EXECUTIVE OFFICE FOR CHEMICAL AND BIOLOGICAL DEFENSE PROGRAMMATIC MISSION AREAS

JPM Biological Defense: Develops, produces, fields and sustains world-class biological defense technology and equipment for the Joint Services. In partnership with the civilian sector, academia and industry, the JPM-BD will ensure that its biological defense products and services are developed at the best possible time, and can be sustained in operation at the lowest life cycle cost.

JPM NBC Contamination Avoidance: The Joint Project Manager for Nuclear, Biological, and Chemical Contamination Avoidance is responsible for the development, production, integration, testing, and fielding of NBC detection, obscuration, and reconnaissance systems. We ensure that our system developments, integration efforts and services focus on the Joint Warfighters' needs within cost, schedule, and performance parameters.

JPM Collective Protection: In Support of the National Military Strategy, research, develop, procure, field, dispose of, and provide sustainment guidance for Collective Protection equipment and systems that protect personnel and equipment within protected areas from chemical, biological, radiological, and toxic industrial materials.

JPM Decontamination: The Joint Project Manager Decontamination (JPM, Decon), Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) is responsible for providing US Forces the capability to sustain operations in a contaminated environment with the least necessary burden and minimum degradation to mission accomplishment.

JPM Guardian: To provide integrated non-conventional and conventional weapon defense capabilities for installation protection and support to civilian authorities

JPM Individual Protection: The JPM IP develops, tests, procures and fields state of the art garments, masks, boots and gloves to protect the Warfighter from chemical, biological and radiological threats. The JPM-IP is the principal advocate and single point of contact for all

acquisition efforts within the Department of Defense for individual protection of chemical and biological threats.

JPM Information Systems: The mission of the Joint Project Manager for Information Systems is to provide the information architecture and applications for shaping the battle space against the chemical and biological threat. The Joint Project Manager for Information Systems provides the war fighter with integrated early warning capability, an accredited hazard prediction model, state-of-the-art consequence management, and course of action analysis tools.

Technical Contact Information:

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JPM Chemical and Biological Medical Systems: The Chemical Biological Medical Systems Joint Project Management Office (CBMS-JPMO) is responsible for the development, procurement, fielding, and sustaining of premier medical protection and treatment capabilities against chemical and biological warfare agents. Our products are all submitted through the U.S. Food and Drug Administration (FDA) licensing or approval processes. The mission of CBMS JPMO is to develop and field FDA-approved medical CBRN countermeasures for the Warfighter. We are seeking proposals in support of this overarching mission. We are interested in proposals that are based on data from experiments using specific CBRN agents, not surrogates, to demonstrate safety, efficacy or mode of action. We are interested in ways to develop medical CBRN countermeasures more rapidly and with increased efficiency through enabling technologies, life cycle bioinformatics, and improved logistics tracking. We are not interested in proof-of-concept, advanced, applied or basic research proposals. We are interested in efforts directed toward the development of enabling technologies that speed up the advanced development process leading to FDA approval. All developmental efforts nominated to be considered by this BAA should be evaluated against the Technology Readiness Levels (TRL) for Medical Product Development (Appendix A). Potential developmental efforts must be consistent with the minimum criteria at TRL level 3-4 for transition to advanced development.

BIOLOGICAL MEDICAL PROPHYLAXIS

Biological Medical Prophylaxis provides medical countermeasures against biological warfare agents. These countermeasures include specialized medical materiel (e.g., vaccines, antivirals, antitoxins, immunotherapeutics) as well as other biological products (e.g., immunoglobulins) designed to be effective as prophylaxis or, to treat rare but serious adverse events from other prophylaxis treatments. Biological Medical Prophylaxis countermeasures must be FDA-approved to provide the Joint Force with the ability to protect Warfighters from the debilitating and life threatening health threats of biological warfare agents (bacteria, viruses, and biotoxins) prior to the appearance of symptoms, thereby protecting Warfighters, conserving the strength of forces, and reducing the impact on the medical care system.

Biological Medical Prophylaxis countermeasures should protect against battlespace challenge of biological warfare agents (BWA) (e.g., aerosol exposure), be deliverable by minimally invasive means in as few doses as feasible, provide protection as quickly as possible, maintain protection as long as possible, be effective against a broad spectrum of agents, and be flexible enough to respond to a wide range of agents, including genetically altered agents. Biological Medical Prophylaxis countermeasures should limit the logistic burden on the force through limited special storage or handling requirements, reduced dosing, administration, and monitoring requirements. These capabilities must also provide for insertion of technology upgrades and commonality of components to address changing threats.

Biological Medical Prophylaxis technologies must be in advanced development, either preclinical or at the clinical evaluation stage of development. Ideally, products should be ready for Investigational New Drug (IND) application to the FDA, or already in or beyond Phase 1 clinical safety trials.

Overarching priorities of the Biological Medical Prophylaxis program include:

1. Develop prophylaxis or pretreatment systems to protect Warfighters from the effects of biological warfare agents prior to the appearance of symptoms. Primary prevention through vaccination is generally preferred as a long term goal, where possible and supported by the nature of the agent. Vaccine development is historically a difficult, expensive, and time-consuming effort. Vaccines are agent, and frequently subtype specific. For these reasons, there is particular interest in broad spectrum protection and multi-agent medical products.

    a. Vaccine development which focuses on protection from agents in aerosol exposure, molecular approaches for development of vaccines, measurement of relevant cellular and humoral protective immune responses, and expression or production of protective antigens using recombinant technology.

    b. Vaccine development for specific toxins and disease agents which could involve the generation, selection and characterization of attenuated strains or inactivated purified antigen preparations, to include polyvalent vaccines that are more broadly effective.

    c. Safer means of passive immunization, such as production of human monoclonal or modified antibodies that are despeciated.

2. Prevention, treatment or supportive care regimens for adverse reactions to prophylaxis or pretreatments. Some vaccines or other pretreatments occasionally result in adverse reactions that require treatment themselves, such as in the case of smallpox vaccine. In such circumstances, an immune globulin or other biological or drug product is required to be part of the vaccine or product "system" to prevent or treat rare but potentially serious adverse events. FDA approval is required for these associated products.

3. Enabling technologies that support, facilitate, or accelerate the development or licensure of Biological Medical Prophylaxis countermeasures.

a. Identification of correlates of protection for the agents described above and development of assays to assess such protection.

b. Development/characterization of relevant animal models to meet FDA licensing requirements for biodefense biologics.

c. Development of improved methods for delivery of vaccines, including adjuvants, nucleic acid vaccines, methods for oral or nasal immunization with inactivated, live and subunit antigens; sustained release formulations; and methods for delivery of antigens for specific induction of mucosal immunity and development of methods to enhance appropriate immune responses to include co-delivery of cytokines.

Infectious agents of interest to the Biological Medical Prophylaxis program include Ebola virus, Marburg virus, poxvirus models of variola virus and those agents causing Venezuelan equine encephalitis, western and eastern equine encephalitis, Tularemia, Q-fever, and Brucellosis. Toxins of interest include those from plants (ricin), bacteria (Staphylococcal enterotoxins, botulinum toxin serotypes C, D, E, F, G), and membrane damaging toxins.

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MEDICAL CHEMICAL DEFENSE

Prophylactic/pretreatment and therapeutic pharmaceuticals, for the purpose of this BAA, are *pharmacological* or *biological* products used to prevent or treat patients exposed to chemical warfare agents (CWA). The products will be licensed or approved by the FDA for their intended use, potentially to include juvenile, geriatric, or immunocompromised patients. Treatment of chemical casualties depends on effective use of multiple medical capabilities in an integrated manner. Warfighters may use self-administered pharmaceuticals or administer pharmaceuticals to another Warfighter. Health care providers must have appropriate pharmaceuticals, tools to diagnose and monitor response of casualties, and appropriate means to protect themselves from chemical hazards. We are particularly interested in developing medical chemical countermeasures that are active against a broad spectrum of chemical agents. Chemical agents of concern fall under the broad categories of nerve, blister, blood, and pulmonary agents.

Overarching goals of the Medical Chemical Defense project include:

1. Develop systems that support maintenance or restoration of pre-CWA exposure health and that allow Warfighters to complete their mission. This includes medical CWA countermeasures that prevent, reverse, or significantly mitigate the effects and negative operational impact of CWA. Medical CWA countermeasures may block the effects of CWA, stop or reverse the direct effects of those agents, or prevent or treat the pathology and symptoms of chemical agents. Specific areas of interest include:

    a. Drug treatment strategies to control seizures produced by nerve agents and protect against the neurological sequelae.

b. CWA pretreatments, prophylactics, or scavengers that can protect the Warfighter from nerve agent exposure and afford protection without physiological side effects.

c. Safe and effective cutaneous prophylactics and therapeutics to treat vesicant (blister) CWA injuries.

d. Safe and effective prophylactics and therapeutics to treat cyanide intoxication (See Category 3, page 16).

2. Develop medical CWA countermeasures that provide broad-spectrum prevention or treatment for classes of chemical agents and a range of exposure routes. Threats from chemical agents are likely to become more complex in the future as a result of increased agent variety and sophistication. Therefore, the products should be flexible enough to respond to a wide range of agents, including traditional and emerging agents. Medical CWA countermeasure systems might also include developing therapies and protocols for treatment that mitigate agent persistence or special effects of new threat agents, such as those that can potentially penetrate protective clothing.

3. Evaluate and leverage enabling technologies to enhance/prolong the shelf life of nerve agent countermeasures currently in the military arsenal. Areas of interest include developing new container-closure systems, wet-dry autoinjectors or formulation development.

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MEDICAL RADIOLOGICAL COUNTERMEASURES (MRC)

The goal of the MRC project is to select, develop, and manufacture FDA-approved drugs and biologics to increase survival and decrease incapacity by treating the incipient or manifest radiation injury following exposure to radiation from nuclear or radiological weapons so that Warfighters can maintain operational effectiveness. MRC must be safe, efficacious, free of performance-degrading side effects, compatible with current military CBRN countermeasures, and usable while in combat or garrison, during medical evacuation, and in hospital. Desired, but not mandatory, product attributes include ease of administration (e.g., autoinjector) and administrable to subjects wearing military protective gear, efficacy with a single dose or short course of treatment, and retained efficacy even if delivered more than 24 hours after radiation exposure. MRC should not require refrigeration or have other significant logistical burdens and should have a relatively long shelf life. These requirements are derived from the "CBRN Agents Therapeutic Pharmaceuticals Initial Capabilities Document," dated July 18, 2005 (JROCM 155-05). *Excluded from consideration under this BAA are candidate MRC which require use prior to exposure (i.e., prophylaxis) and next generation antibiotics and probiotics, blocking, decorporation, and purgative agents, antiemetics and other comfort or supportive measures.*

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MEDICAL DIAGNOSTIC SYSTEMS

The DoD has a need for technologies for the detection, identification, and clinical diagnosis of infection by pathogens and toxins with the potential to negatively impact force health and effectiveness. Sensitivity, specificity, ease of use, and deployability (size, weight, power requirements, reduced consumables) are critical features of such systems. An integrated system using multiple technology approaches that will reduce the potential for misdiagnosis of a BWA or other disease agent in clinical samples will provide the solution for future diagnostic capabilities. Specific areas of interest include:

1. Increase the capability of current diagnostic systems via the addition of functional modules.

2. Technologies or concepts which will decrease system size, weight, procurement and life cycle cost, logistics footprint, and training requirements.

3. Cross-over technologies such as diagnostics applicable to both clinical diagnosis of disease caused by both BWA and militarily-relevant infectious diseases and environmental monitoring (including the detection of food-borne pathogens).

4. Population health monitoring including a) real-time, b) predictive models, and c) expert systems.

5. Novel nucleic acid-based assays for BWA to include clinical, food, and environmental samples.

6. Novel non-nucleic acid-based assays for BWA, food pathogens, and toxins, including but not limited to immunoassays or novel detection reagents (e.g., antibodies or non-antibody recognition reagents).

7. Technologies or methods for the detection of pathogens and toxins of DoD interest, including BWA, that reduce or eliminate the need for analyte-specific reagents.

8. Systems or methods for analytical sample preparation compatible with nucleic acid-based (DNA and RNA) and non-nucleic acid-based detection methods, with emphasis on simplified methods that enrich and concentrate target analytes. Manual and automated systems are of interest, with a particular focus on automated methods that can be integrated with analytical platforms.

9. Methods for stabilizing analytical reagents at room temperature (e.g., 22-28° C and elevated temperatures up to 50° C).

10. Development and validation of host response biomarkers of infection or disease that permit diagnosis of infection while still in the presymptomatic or very early symptomatic phase when intervention is most likely to be effective.

11. Development of assays for validated host response biomarkers of infection or disease that are compatible with, and can be transitioned to, potential next generation diagnostic technologies.

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JPEO/ CBMS JPMO CATEGORIES OF INTEREST FOR THIS BAA

CATEGORY 1. MEDICAL CBRN COUNTERMEASURE PROTOTYPES

To obtain and develop the best Medical CBRN Countermeasure technologies, regardless of their source, the CBMS JPMO is contemplating the use of Prototype OTs for the purpose of developing medical CBRN Countermeasure prototypes. Nontraditional defense contractors, including large pharmaceutical companies, are eligible to submit a proposal for medical CBRN countermeasure prototype development under this BAA.

A nontraditional defense contractor is a business unit that has not, for a period of at least one year prior to the date of the OT agreement, entered into or performed on (1) any procurement contract that is subject to full coverage under the cost accounting standards prescribed pursuant to section 26 of the Office of Federal Procurement Policy Act (41 USC 422) and the regulations implementing such section; or (2) any other procurement contract in excess of $500,000 to carry out prototype projects or to perform basic, applied, or advanced research projects for a federal agency.

For a candidate medical CBRN Countermeasure to be eligible for consideration for development through FDA approval as a prototype under this BAA, it must be the subject of an active IND application with the FDA that is not on clinical hold. The IND may be for an indication other than the indication to be obtained as part of the proposed effort. The advanced development of a MRC requires the capability to build the necessary processes to select, develop, validate and manufacture a drug or biologic in accordance with FDA current Good Manufacturing Practices (cGMP) regulations and guidelines. **Therefore, medical CBRN countermeasure prototype proposals (and white papers/preproposals) submitted in response to this BAA must provide substantiated *in vivo* safety and efficacy data arising from the study of the proposed CBRN countermeasure candidate, evidence of compliance with cGMP, and evidence of good management skills and practices.**

1. Advanced development of MRC prototypes through FDA approval. This effort may include clinical safety studies, pivotal efficacy studies, small and large scale manufacturing, and the preparation and submission of a New Drug Application (NDA) or Biologic License Application (BLA) to the FDA. Please see the Special Instruction below regarding MRC prototypes of interest.

2. Develop medical countermeasures against a broad spectrum of CWA (e.g., nerve and blister agents) by identifying and characterizing compounds or medical strategies

using laboratory and animal models that demonstrate the ability to prevent, interrupt, or terminate the action of CWA.

CATEGORY 2. SPECIAL PROJECTS

The CBMS JPMO is frequently provided funding identified by Congressional committees for special interest developmental efforts relating to medical CBRN countermeasures, enabling technologies, life cycle bioinformatics, health-care delivery; to detection, diagnosis, control or eradication of specified diseases, conditions, or syndromes; or to other initiatives relevant to health needs. Funding of these areas is contemplated to be by grant and is dependent upon Congressional direction and availability of funds.

1. Evaluation of adult-derived stem cells for the repair of tissues following exposure to doses of ionizing radiation sufficient to cause acute radiation syndrome.

2. Evaluation of oral formulations vaccines efficacious against multiple BWA.

3. Comparative performance evaluation of novel, rapid molecular diagnostic assays against unique field isolates of bacterial BW pathogens and food-borne pathogens of military concern.

4. Evaluation of novel pretreatment drugs or compounds which, when taken prior to CWA exposure, increase the efficacy of fielded or developmental medical chemical therapeutic countermeasures.

5. Evaluation of measures to improve the safety or immunogenicity profiles of investigational or licensed vaccines.

CATEGORY 3. DEVELOPMENTAL PROCUREMENT INITIATIVES SUPPORTING MEDICAL CBRN COUNTERMEASURES AND ENABLING TECHNOLOGIES

1. Conduct Good Laboratory Practices (GLP)-compliant *in vivo* studies to demonstrate the safety, efficacy, pharmacokinetics and pharmacodynamics of candidate medical CBRN countermeasures. The study endpoint should be clearly related to the desired benefit in humans in accordance with the FDA "Animal Rule" (21 CFR 314 [I] or 21 CFR 601 [H]).

2. Identifiy and characterize the mechanism of action of candidate medical CBRN countermeasures. Mechanism of action data are required to satisfy the requirements for FDA approval under the "Animal Rule".

3. Conduct of Phase 1 clinical safety studies of potential candidate medical CBRN countermeasures.

4. Evaluate manufacturing processes which may improve the production, shelf life, or stability of candidate or FDA-approved medical CBRN countermeasures.

5. Evaluate novel technologies which a) enable or facilitate efficacious medical logistics cold-chain management and b) eliminate or reduce cold chain requirements for medical CBRN countermeasure storage or shipment.

6. Evaluate emerging life cycle bioinformatics technologies for the ability to improve management processes throughout the discovery, preclinical research, manufacturing, and clinical evaluation phases of pharmaceutical development.

7. Evaluate enabling technologies to enhance/prolong the shelf life of medical CBRN countermeasures currently in the military inventory, including new container-closure systems, wet-dry autoinjectors, or formulations.

8. Evaluate enabling models and simulations, including predictive models and expert systems for population health monitoring.

9. Test and develop products with minimal logistical burden. Activities include development of formulations that require minimal refrigeration, possess long regulatory shelf life, and long operational life once issued. Desired product characteristics would include administration in a single dose, to reduce the need for re-dosing and the ability to use during patient transportation and evacuation as appropriate.

CATEGORY 4. OTHER

Whether under procurement contract, grant or Prototype OT, any other element of developmental effort that would foster or enhance the prospect of potential new products that are consistent with the programmatic mission areas described in The CBMS JPMO Programmatic Mission Area which may be suitable for future competitive advanced development procurements.

CATEGORY 5. DETECTION, DECONTAMINATION AND INFORMATION SOLUTIONS

Identify, mature, and insert science and technology efforts that cut across capabilities, provide substantial improvement to the current state-of-the-art, and add more capability value. The JPEO is specifically interested in research and development of the following capabilities (in order of importance):

- Automated, multi-platform sample preparation
  - Reduce operator error
  - Increase ID confidence
  - Provide independent datapoint
  - Decrease time to obtain results

- Chemical stand-off detection and identification
  - Reduce false positives
  - Enhance performance on low volatility agents
  - Reduce time to detect and ID

- Decontamination solutions:
  - Non-peroxide based
  - For Non-Traditional Agents (NTAs)

- Biological warfare agent stand-off detection and identification
  - Provide 24/7 capability
  - Increase sensitivity
  - Reduce time to warn

- Biological warfare agent point detection
  - Reduced costs
  - Increase sensitivity
  - Increase specificity
  - Layered network capability

- Improved respiratory Toxic Industrial Chemical (TIC) and NTA filtration
  - Increase personnel protection factor
  - NIOSH compliance

- Chemical agent point detection
  - Increase sensitivity
  - Increase specificity
  - Layered network capability

- Fabric technology eliminating the need for chemical and biological protective overgarments and improved collective protection

- Integrated early warning

- Improved radiological detection and identification

- Medical therapeutics and/or prophylaxis for NTAs

- Test and evaluate chemical warfare vapor detectors (CWVD) to validated test methods that are aligned with requirements. Develop and validate additional CWVD test methods and requirements. Assist with CWVD certification and accreditation program by supplying technical recommendations for completing the strategies going forward.

- Open community-of-interest medical and Chemical, Biological, Radiological, and Nuclear (CBRN) data sharing between medical and CBRN information systems

Technology Readiness Levels for Medical Countermeasure Products (Drugs and Biologics)[1,2]

Note: When using this schematic, a medical countermeasure product should be rated at a particular level only after the sponsor has completed all activities listed in that level (i.e., a product is rated at TRL 4 until it completes all activities listed in TRL 5).

TRL	Integrated Medical Countermeasure TRLs *(based on October 2004 DoD Medical TRLs and May 2008 PHEMCE TRLs)*
1	**Review of Scientific Knowledge Base** Active monitoring of scientific knowledge base. Scientific findings are reviewed and assessed as a foundation for characterizing new technologies.
2	**Development of Hypotheses and Experimental Designs** Scientific "paper studies" to generate research ideas, hypotheses, and experimental designs for addressing the related scientific issues. Focus on practical applications based on basic principles observed. Use of computer simulation or other virtual platforms to test hypotheses.
3	**Target/Candidate Identification and Characterization of Preliminary Candidate(s)** Begin research, data collection, and analysis in order to test hypothesis. Explore alternative concepts, identify and evaluate critical technologies and components, and begin characterization of candidate(s). Preliminary efficacy demonstrated *in vivo*. **3A** Identify target and/or candidate. **3B** Demonstrate *in vitro* activity of candidate(s) to counteract the effects of the threat agent. **3C** Generate preliminary *in vivo* proof-of-concept efficacy data (non-GLP).

[1] This document is designed for evaluating the maturity of medical countermeasure development programs. For a detailed description of development processes for assays and animal models, please consult the Technology Readiness Levels for Product Development Tools (PDTs), developed by the PDT Working Group of the HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE).

[2] This document does not serve as official FDA Guidance. For the purposes of a regulatory application seeking licensure or approval for a specific medical product, additional data may be required by FDA.

TRL	Integrated Medical Countermeasure TRLs *(based on Oct 2004 DoD Medical TRLs and May 2008 PHEMCE TRLs)*
4	**Candidate Optimization and Non-GLP *In Vivo* Demonstration of Activity and Efficacy** Integration of critical technologies for candidate development. Initiation of animal model development. Non-GLP *in vivo* toxicity and efficacy demonstration in accordance with the product's intended use. Initiation of experiments to identify markers, correlates of protection, assays, and endpoints for further non-clinical and clinical studies. *Animal Models:* Initiate development of appropriate and relevant animal model(s) for the desired indications. *Assays:* Initiate development of appropriate and relevant assays and associated reagents for the desired indications. *Manufacturing:* Manufacture laboratory-scale (i.e. non-GMP) quantities of bulk product and proposed formulated product. **4A** Demonstrate non-GLP *in vivo* activity and potential for efficacy consistent with the product's intended use (i.e. dose, schedule, duration, route of administration, and route of threat agent challenge). **4B** Conduct initial non-GLP toxicity studies and determine pharmacodynamics and pharmacokinetics and/or immune response in appropriate animal models (as applicable). **4C** Initiate experiments to determine assays, parameters, surrogate markers, correlates of protection, and endpoints to be used during non-clinical and clinical studies to further evaluate and characterize candidate(s).

TRL	Integrated Medical Countermeasure TRLs *(based on Oct 2004 DoD Medical TRLs and May 2008 PHEMCE TRLs)*
5	**Advanced Characterization of Candidate and Initiation of GMP Process Development** Continue non-GLP *in vivo* studies, and animal model and assay development. Establish draft Target Product Profiles. Develop a scalable and reproducible manufacturing process amenable to GMP. *Animal Models:* Continue development of animal models for efficacy and dose-ranging studies. *Assays:* Initiate development of in-process assays and analytical methods for product characterization and release, including assessments of potency, purity, identity, strength, sterility, and quality as appropriate. *Manufacturing:* Initiate process development for small-scale manufacturing amenable to GMP. *Target Product Profile:* Draft preliminary Target Product Profile. Questions of shelf life, storage conditions, and packaging should be considered to ensure that anticipated use of the product is consistent with the intended use for which approval will be sought from FDA. **5A** Demonstrate acceptable Absorption, Distribution, Metabolism and Elimination characteristics and/or immune responses in non-GLP animal studies as necessary for IND filing. **5B** Continue establishing correlates of protection and/or surrogate markers for efficacy for use in future GLP studies in animal models. Identify minimally effective dose to facilitate determination of "humanized" dose once clinical data are obtained.
6	**GMP Pilot Lot Production, IND Submission, and Phase 1 Clinical Trial(s)** Manufacture GMP pilot lots. Prepare and submit Investigational New Drug (IND) package to FDA and conduct Phase 1 clinical trial(s) to determine the safety and pharmacokinetics of the clinical test article. *Animal Models:* Continue animal model development via toxicology, pharmacology, and immunogenicity studies. *Assays:* Qualify assays for manufacturing quality control and immunogenicity, if applicable. *Manufacturing:* Manufacture, release and conduct stability testing of GMP bulk and formulated product in support of the IND and clinical trial(s). *Target Product Profile:* Update Target Product Profile as appropriate. **6A** Conduct GLP animal studies for toxicology, pharmacology, and immunogenicity as appropriate. **6B** Prepare and submit full IND package to FDA to support initial clinical trial(s). **6C** Complete Phase 1 clinical trial(s) that establish an initial safety and pharmacokinetics assessment.

TRL	Integrated Medical Countermeasure TRLs *(based on Oct 2004 DoD Medical TRLs and May 2008 PHEMCE TRLs)*
7	**Scale-up, Initiation of GMP Process Validation, and Phase 2 Clinical Trial(s)[3]** Scale-up and initiate validation of GMP manufacturing process. Conduct animal efficacy studies as appropriate[4]. Conduct Phase 2 clinical trial(s)[3]. *Animal Models:* Refine animal model development in preparation for pivotal GLP animal efficacy studies. *Assays:* Validate assays for manufacturing quality control and immunogenicity if applicable. *Manufacturing:* Scale-up and validate GMP manufacturing process at a scale compatible with USG requirements. Begin stability studies of the GMP product in a formulation, dosage form, and container consistent with Target Product Profile. Initiate manufacturing process validation and consistency lot production. *Target Product Profile:* Update Target Product Profile as appropriate. **7A** Conduct GLP animal efficacy studies as appropriate for the product at this stage[4]. **7B** Complete expanded clinical safety trials as appropriate for the product (e.g., Phase 2)[3].

[3] Identification of later regulatory stages of clinical development in this document (e.g., Phase 2, Phase 3) may not apply to some products being developed under the 'Animal Rule'. Other than human safety and pharmacology studies, no additional clinical data may be feasible or ethical to obtain.

[4] These could include GLP animal efficacy studies required by FDA at this stage in support of an Emergency Use Authorization (EUA). Requirements for issuance of an EUA will be handled on a case-by-case basis and will depend on the nature and extent of the threat at any point during the product development timeline, from the initiation of Phase 1 studies through licensure or approval. GLP animal efficacy study requirements may also vary by product type (e.g., vaccine, therapeutic, prophylactic) and U.S. government agency program office.

TRL	Integrated Medical Countermeasure TRLs *(based on Oct 2004 DoD Medical TRLs and May 2008 PHEMCE TRLs)*
8	**Completion of GMP Validation and Consistency Lot Manufacturing, Pivotal Animal Efficacy Studies or Clinical Trials[3], and FDA Approval or Licensure** Finalize GMP manufacturing process. Complete pivotal animal efficacy studies or clinical trials (e.g., Phase 3), and/or expanded clinical safety trials as appropriate. Prepare and submit NDA/BLA. *Manufacturing:* Complete validation and manufacturing of consistency lots at a scale compatible with USG requirements. Complete stability studies in support of label expiry dating. *Target Product Profile:* Finalize Target Product Profile in preparation for FDA approval. **8A** Complete final pivotal GLP animal efficacy studies or pivotal clinical trials (e.g., Phase 3), and any additional expanded clinical safety trials as appropriate for the product[3]. **8B** Prepare and submit New Drug Application (NDA) or Biologics Licensing Application (BLA) to the FDA. **8C** Obtain FDA approval or licensure.
9	**Post-Licensure and Post-Approval Activities** **9A** Commence post-licensure/post-approval and Phase 4 study commitments, such as safety surveillance, data to support use in special populations, and clinical trials to confirm safety and efficacy as feasible and appropriate[5]. **9B** Maintain manufacturing capability as appropriate.

[5] For products approved under the 'Animal Rule', confirmatory efficacy data is required and may be obtained from use during an event.